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Lithium acetylides, generated from terminal acetylenes with n-BuLi in THF at –70 ºC, react chemoselectively with ω-haloalkyl tosylate in the presence of 10 mole % of Bu4I at 70 ºC to furnish ω-haloalkyl acetylenes in very good yields. The ω-haloalkyl acetylenes were subject to intra-molecular alkylation with LDA to provide dicycloalkylethyne

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An Efficient Synthesis of Dicycloalkylacetylenes: 1, 2-Dicyclopropylethyne and (cyclopropylethynyl)cyclobutane (Preprint)

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Lithium acetylides, generated from terminal acetylenes with n-BuLi in THF at – 70 ºC, react chemoselectively with ω-haloalkyl tosylate in the presence of 10 mole % of Bu_4I at 70 ºC to furnish ω-haloalkyl acetylenes in very good yields. The ω-haloalkyl acetylenes were subject to intra-molecular alkylation with LDA to provide dicycloalkylethyne

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The classic methods for the synthesis of terminal/internal alkynes involve the alkynylation of alkylhalide with metal acetylide[1] or base promoted dehydrohalogenation[2] of vicinal dihalide/vinyl halide. Programatically, our research interest is directed towards 1,2-dicycloalkylacetylenes having ring strain cyclopropyl and/or cyclobutyl groups. The synthesis of 1,2-dicycloalkylalkyne can be achieved either by generation of the acetylene bond in an appropriate precursor having a cycloalkyl group or by constructing the cycloalkyl group via intramolecular alkylation of the appropriate ω-haloalkyl acetylenic compound. The synthesis of 1,2-dicyclopropylethyne has been reported in the literature involving internal alkylation of ω-haloalkylethyne forming cyclopropyl group[3]

and via rearrangement[4] or elimination[5] of a suitable precursor to generate the acetylenic bond. The synthesis of dicyclobutylethyne is not reported in the literature. However, Handy and Benson synthesized bis(tetrahalocyclobutyl)ethyne[6] via condensation of divinylethyne with tetrafluoro- and chlorotrifluoroethylene at high temperature (~150 °C) under self generated pressure in a sealed vessel. Salaun, Fadel and Conia[7] reported (cyclopropylethynyl)cyclobutane derivative , 2-(cyclopropylethynyl)cyclobutanone via ring enlargement of the 1-(3-cyclopropyl-1-hydroxyprop-2-ynyl)cyclopropanol.

The internal carbocyclization approach is more promising then the rearrangement and elimination processes as it does not require any exotic starting materials and is largely free from any by-product. ω-Haloalkylalkyne precursors are required for internal cyclization to furnish dicycloalkyalkynes. Meijere et al. introduced cyclopropyl rings via intra molecular alkylation[3] of the 1,8-dichlorooct-4-yne[8] using lithium diisopropylamide (LDA). However, the alkynylation of dihaloalkane with metal acetylide suffers from low yield as is evident from the reported synthesis of 5-chloropent-1-yne (**5**, 57%)[9] and 1,8-dichlorooct-1-yne(**9**, 36%).[8] We report here an efficient and economical synthesis of dicycloalkylethynes namely 1,2-dicyclopropyl-ethyne (**16**) and (cyclopropylethynyl)cyclobutane (**17**).

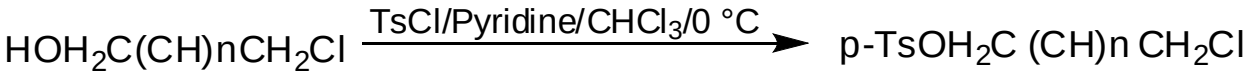
Conventionally, alkynylation of haloalkanes is carried out using metal acetylides in liquid NH_3 having HMPA or DMPU as co-solvent.[1] Chong and Buck[10] observed that the presence of sodium iodide (NaI) or tetrabutylammonium iodide (Bu_4I) in catalytic amounts (10 mol %) had a spectacular effect on the reaction of lithium acetylides with primary halides (X = Br or Cl) which otherwise exhibited very sluggish and incomplete reactions in tetrahydrofuran (THF) solution thus eliminating health hazard chemical. The difference in reactivity between triflate and bromide groups in the SN_2 reaction with ω-bromoalkyl triflates led Chong et al. to synthesize unsymmetrical non-conjugated diynes[11] by chemoselective monoalkynylation of ω-bromoalkyl triflates with alkynyllithium followed by another alkynylation of the resulting bromoalkyne with alkynyllithium in the presence of 10 mol % NaI.

ω-Halocycloalkyl/ω-dihaloalkyl alkynes, precursors for 1,2-dicycloalkylacetylenes, are required for internal carbocyclization. The alkynylation reaction of 1-bromo-3-chloropropane/1-bromo-4-chlorobutane in THF was very sluggish and incomplete. However, the reaction in the presence of 10 mol % Bu_4NI furnished inseparable mixtures of corresponding bromo- and

chloroalkylalkynes. Taking advantage of chemoselectivity between the tosylate and chloro group in the SN_2 reaction, ω-chloroalkyl tosylates (**3** & **4**) are used for alkynylation to avoid mixture formation.

Tosylation of ω-Haloalkyl Alcohols (1 & 2): The 3-chloropropyl-4-methylbenzenesulfonate (**3**)[12] and 4-chlorobutyl-4-methylbenzenesulfonate (**4**)[13] were prepared from 3-chloropropanol (**1**) and 4-chlorobutanol (**2**), respectively, by using alcohol/ tosyl chloride/ pyridine in 1: 1.5: 2 ratio respectively developed[14] by Kabalka et al. (**Scheme**-1). The yield of **3** improved to 95%.

Scheme 1: Tosylation of ω-Haloalkyl Alcohols

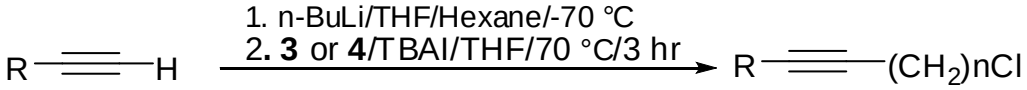


1. n = 1; X = Cl
2. n = 2; X = Cl

3. n = 1; X = Cl (95%)
4. n = 2; X = Cl (85%)

Chemoselective alkynylation of ω-chloroalkyl tosylates (3 & 4): Whitley et al. performed[12] alkynylation of **3** in THF under phase-transfer condition using stochiometric quantity of n-Bu_4NBr. However, we adopted catalytic phase-transfer methodology[10,11] developed by Chong. Treatment of lithium acetylides generated in situ from alkynes **5**-**8** in THF and n-butyllithium (2.5 M hexane n-BuLi) at -70 °C, with ω-chloroalkyl tosylates 3 or 4 in the presence of 10 mole % of n-Bu_4NI at 70 °C furnished single ω-chloroalkylated acetylenes **9**-**15** in the range of 50-80% yield (**Scheme**-2).

SCHEME 2: Alkynylation of ω-Haloalkyl Tosylates



5. R = $Cl(CH_2)_3$ -
6. R = $Cl(CH_2)_4$ -
7. R = cy-C_3H_5 -
8. R = cy-C_4H_7 -

9. R = $Cl(CH_2)_3$ -; n = 3 (66%)
10. R = $Cl(CH_2)_4$ -; n = 3 (56%)
11. R = $Cl(CH_2)_4$ -; n = 4 (51%)
12. R = cy-C_3H_5 -; n = 3 (80%)
13. R = cy-C_3H_5 -; n = 4 (73%)
14. R = cy-C_4H_7 -; n = 3 (72%)
15. R = cy-C_4H_7 -; n = 4 (73%)

Intramolecular cyclization of ω-Haloalkylated Acetylenes (9-15): Intramolecular cyclization by generating a carbon nucleophile adjacent to an

acetylenic bond of a ω-haloalkylated acetylene is adopted to furnish 1,2-dicycloalkylethyne.

1,2-Dicyclopropylethyne (**16**):Treatment of 1,8-dichloro-oct-4-yne (**9**) and (5-chloropent-1-ynyl)cyclopropane (**12**) with an appropriate quantity (vide experimental) of freshly prepared LDA furnished 1,2-dicyclopropylethyne (**16**) in 92% & 85% yield respectively (**Scheme-3**).

Scheme 3: Intramolecular cyclization of ω-Haloalkylated Acetylenes

(cyclopropylethynyl)cyclobutane (**17**): Exposure of (5-chloro-1-ynyl)cyclobutane (**14**) to 3.1 equivalent of LDA furnished 75% of 1-cyclobutyl-2-cyclopropylacetylene (**17**). However, treatment of 1,9-dichloro-4-nonyne (**10**) with 4.1 equivalent of LDA furnished (6-chlorohex-1-ynyl)cyclopropane (**13**) at low temperature (~0 °C). The 6-chlorohex-1-ynyl moiety in **13** failed to cyclize with LDA to furnish **17** at 0 °C. Warming the reaction mixture to room temperature (~22 ºC) affords a complex mixture of products after workup of the reaction.

1,2-Dicyclobutylacetylene (**18**): Treatment of **11** and **15** with appropriate quantity of LDA failed to furnish 1,2-dicyclobutylacetylene (**18**). Our attempts to cyclize the 6-chlorohex-1-ynyl group to a cyclobutyl group using a Hauser base[15] at an elevated temperature (~77 °C) as reported in the literature[16] also failed. These results further corroborate the earlier findings[17] of non competitiveness of cyclobutyl group formation with dehydrohalogenation and allene-acetylene rearrangement.

In conclusion, we have developed a very efficient and cost effective synthesis for alknylation of ω-chloroalkyl tosylates. The yield of 1,8-dichloro-4-octyne, precursor for 1,2-dicyclopropylethyne, has been improved dramatically by application of the phase-transfer catalyst Bu_4NI(vide supra). The yield of 1,2-dicyclopropylethyne is further improved using 4.1 vs. 2.1 equivalent of LDA as reported[3] in the literature. The alkynylation and intramolecular alkylation

methodologies has been successfully applied towards the synthesis of hybrid (cyclopropylethynyl)cyclobutane (**17**).

Experimental Section

General Procedure for Tosylation of ω-Haloalkyl Alcohols: To cold (~ 0 °C) 1M chloroform solution of ω-haloalkyl alcohols (1 equivalent) is added pyridine (2 equivalents) followed by addition of p-toluenesulfonyl chloride (1.5 equivalents) in small portions with stirring. After completion of the reaction, the reaction mixture is quenched with water and extracted with ether. The organic layer is washed successively with aq. 2N HCl, 5% aq. $NaHCO_3$ and water till water layer is neutral. The organic layer is dried over anhydrous $MgSO_4$, evaporated and the resulting solution is purified by silica gel column using 2% ether/petroleum ether to furnish ω-haloalkyl tosylates.

3-Chloropropyl-4-methylbenzenesulfonate (**3**): IR (neat) 2970, 1598, 1364, 1189, 1177, 1097, 936 cm^{-1}; ^1H NMR(400 MHz, CDCl3) δ 7.80 (2H, d, J = 8 Hz, ArH), 7.37 (2H, d, J = 8 Hz, ArH), 4.2 (2H, t, J = 6 Hz, $-CH_2OSO_2Cl$) , 3.6 (t, J = 6 Hz, $-CH_2Cl$), 2.4 (3H, s, $ArCH_3$), 2.1 (2H, q, J = 6 Hz, $-CH_2-CH_2-CH_2-$); ^{13}C NMR(400 MHz, $CDCl_3$) δ 145.2, 132.9, 130.1, 128.1, 67.0, 40.5, 31.9, 21.9. Anal. Calcd for $C_{10}H_{13}SO_3Cl$: C, 48.29; H, 5.27. Found: C, 48.24; H, 5.23.

4-Chlorobutyl-4-methylbenzenesulfonate (**4**): IR (neat) 2961, 1598, 1358, 1189, 1176, 1097, 934 cm^{-1}; ^1H NMR(400 MHz, $CDCl_3$) δ 7.79 (2H, d, J = 8 Hz, ArH), 7.36 (2H, d, J = 8 Hz, ArH), 4.06 (2H, $-CH_2OSO_2Cl$), 3.5 (2H,$-CH_2Cl$), 2.45 (3H, s, $ArCH_3$), 1.82 (4H, m, $-CH_2CH_2CH_2CH_2-$); ^{13}C NMR(400 MHz, $CDCl_3$) δ 145.1, 133.0, 130.1, 128.0, 69.7, 44.2, 28.6, 26.4, 21.8. Anal. Calcd for $C_{11}H_{15}SO_3Cl$: C, 50.28; H, 5.75. Found: C, 50.34; H, 6.06.

General Procedure for Alkynylation of ω-Haloalkyl Tosylates: To a cold (-70 °C) THF solution of ω-Haloalkyl/cycloalkyl alkyne (1.1 equivalent) is added drop-wise n-BuLi (2.5M solution in hexane, 1 equivalent) during a period of 30 minutes. The solution is allowed to warm to room temperature. A solution of ω-haloalkyl tosylates (0.96 equivalent) in THF followed by tetrabutylammonium iodide (10 mole %) is added to the reaction flask. The reaction mixture is warmed to 70 °C for 2-3 hr when the reaction mixture turns thick. The reaction mixture was monitored by GC for consumption of ω-haloalkyl tosylates. The reaction mixture is cooled to 0 °C, quenched with saturated NH_4Cl and extracted with ether (30 mL x 3). The ether layer is washed sequentially with water till water layer is neutral, aqueous potassium thiosulfate, brine and dried over

anhydrous $MgSO_4$. The liquid obtained after removal of ether, is purified by Kugelrohr or by freeze-thaw distillation.

1,8-Dichlorooct-4-yne (**9**): IR (neat) 2960, 2872, 2916, 1441, 1355 cm^{-1}; ^1H NMR (400 MHz, CDCl3) δ 3.66 (4H, t, J = 6.4 Hz), 2.34(4H, t, J = 6.8 Hz), 1.94 (4H, m); ^{13}C NMR(400 MHz, $CDCl_3$) δ 79.5, 44.0, 31.8, 16.4; Anal. Calcd for $C_8H_{12}Cl_2$: C, 53.65; H, 6.75. Found: C, 51.83; H = 6.75.

1,9-Dichlorononon-4-yne (**10**): IR (neat) 2957, 2868, 2844, 1434, 1291, 726 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.65 (2H, t, J = 6.4 Hz), 3.57 (2H, t, J = 6.6 Hz), 2.39-2.31(2H, m), 2.24-2.216(2H, m), 1.99-1.91(2H, m), 1.91-1.83(2H, m), 1.70-1.59(2H, m); ^{13}C NMR(400 MHz, $CDCl_3$) δ 80.6, 79.0, 44.8, 44.0, 31.9, 31.8, 26.3, 18.2, 16.4. Anal. Calcd for $C_9H_{14}Cl_2$: C, 55.98; H, 7.31. Found: C, 56.30; H = 7.53.

1,10-Dichlorodec-5-yne (**11**): IR (neat) 2947, 2866, 2843, 1453, 1434, 1301, 729 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.57 (4H, t, J = 6.7 Hz), 2.20 (4H, tt, J = 7.0, 2.2 Hz), 1.94-1.84(4H, m), 1.69-1.59(4H, m); ^{13}C NMR(400 MHz, $CDCl_3$) δ 80.2, 44.8, 31.8, 26.4, 18.3. Anal. Calcd for $C_{10}H_{16}Cl_2$: C, 57.98; H, 7.79. Found: C, 58.12; H = 7.91.

(5-Chloropent-1-ynyl)cyclopropane (**12**): IR (neat) 3093, 3011, 2960, 1434, 1362, 1291, 1052, 1040, 1027, 880, 812 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.63 (2H, t, J = 6.4 Hz), 2.31 (2H, t, J = 6.8 Hz), 1.91 (2H, m), 1.91 (1H, m), 0.68-0.75 (2H, m), 0.57-0.64 (2H, m); ^{13}C NMR(400 MHz, $CDCl_3$) δ 88.6, 73.7, 44.0, 32.0, 16.4, 8.2 (2C), -0.3; Anal. Calcd for $C_8H_{11}Cl$: C, 67.37; H, 7.77. Found: C, 66.61; H = 7.78.

(6-Chlorohex-1-ynyl)cyclopropane (**13**): IR (neat) 3092, 3011, 2946, 2234, 1453, 1360, 1301, 1051, 1028, 812 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.56 (2H, t, J = 6.6 Hz), 2.18 (2H, dt, J = 6.9 & 1.6 Hz), 1.93-1.81 (2H, m), 1.67-1.53 (2H, m), 1.25-1.15 (1H, m), 0.75-0.55 (4H, m); ^{13}C NMR (400 MHz, $CDCl_3$) δ 83.9, 74.7, 44.7, 31.6, 26.2, 18.1, 8.0, -0.5; Anal. Calcd for $C_9H_{13}Cl$: C, 69.00; H, 8.36. Found: C, 68.53; H = 8.45

(5-Chloropent-1-ynyl)cyclobutane (**14**): IR (neat) 2983, 2944, 2865, 1437, 1334, 1290, 724 cm^{-1}; ^1H NMR (400 MHz, CDCl3) δ 3.65 (2H, t, J = 6.5 Hz), 3.03-2.91 (1H, m), 2.37 (2H, dt, J = 6.8 Hz, 2.2 Hz), 2.28-2.16 (2H, m), 2.12-1.99 (2H, m), 1.98-1.78 (4H, m); ^{13}C NMR (400 MHz, $CDCl_3$) δ 85.6, 79.0, 44.0, 32.0, 30.3 (2C), 25.3, 19.3, 16.5. Anal. Calcd for $C_9H_{13}Cl$: C, 69.00; H, 8.36. Found: C, 68.58; H, 8.50.

(6-Chlorohex-1-ynyl)cyclobutane (**15**): IR (neat) 2983, 2943, 2864, 1444, 1336, 1315,1301, 728 cm^{-1}; ^1H NMR (400 MHz, CDCl3) δ 3.59 (2H, t, J = 6.6

Hz), 2.98 (1H, m, cyclobutyl CH), 2.28-2.18 (4H, m), 2.12-2.00 (2H, m), 1.96-1.79 (4H, m), 1.69-1.59 (2H, m); ^{13}C NMR (400 MHz,$CDCl_3$) δ 85.19, 80.24, 44.90, 31.80, 30.40, 26.42, 25.34, 19.33, 18.38; Anal. Calcd for $C_{10}H_{15}Cl$: C, 70.37; H, 8.86. Found: C, 70.34; H, 8.84.

General Procedure for Intramolecular cyclization of ω-Haloalkylated Acetylenes: To a dry THF solution of diisopropylamine (1 equivalent) is added n-BuLi (2.5 M in hexane, 1 equivalent) at -70 °C during a period of one hour. The lithium diisopropylamide solution is brought to -10 °C over a period of time. The LDA solution is transferred via cannula to a jacked dropping funnel at 0 °C. The LDA solution is added to a stochiometric solution of ω,ω´-dihaloalkyl/ω-haloalkyl alkynes in dry THF at -70 ºC during 45 minutes. The reaction mixture is allowed to warm up to 0 °C when the GC indicates the completion of the reaction. The reaction mixture is poured on to saturated aqueous NH_4Cl solution. The mixture is extracted with n-pentane. The organic layer is washed sequentially with 2% aqueous HCl, aqueous $NaHCO_3$, water till aqueous layer is neutral (pH ≈ 7) and brine solution. The organic layer is dried over anhydrous $MgSO_4$. Removal of solvent furnishes liquid which is subjected to freeze-thaw distillation.

1,2-Dicyclopropylethyne (**16**): (a) From 1,8-Dichloro-4-Octyne (**9**) and (b) From (5-chloropent-1-ynyl)cyclopropane (**12**): IR (neat) 3092, 3012, 1425, 1377, 1216, 1051, 1002, 829, 811cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.21-1.12 (m, 2H), 0.71-0.63 (4H, m), 0.63-0.; ^{13}C NMR (400 MHz, $CDCl_3$) δ 78.93, 8.21, -0.30; Anal. Calcd for C_8H_{10}: C, 90.51; H, 9.49. Found: C, 89.61; H, 9.49.

(**Cyclopropylethynyl)cyclobutane (17)**: Freeze-thaw distillation; 75% yield. IR (neat) 3092, 2982, 2944, 2865, 1363, 1050, 1026, 976, 909, 810 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.01-2.90 (1H, m), 2.26-2.15 (2H, m), 2.12-1.99 (2H, m), 1.94-1.77(2H, m), 1.30-1.18(1H, m), 0.76-0.69 (2H, m), 0.65-0.59 (2H, m); ^{13}C NMR (400 MHz, $CDCl_3$) δ 84.22, 79.89, 30.41 (2C, CH_2), 25.38, 19.27, 8.35 (2C, CH_2), -0.18; Anal. Calcd for C_9H_{12}: C, 89.94; H10.06. Found: C, 89.90; H, 10.07.

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Supporting Information Available: Experimental procedures and copies of NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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SUPPORTING INFORMATION:

EXPERIMENTAL

Ethynylcyclopropane (**7**) and ethynylcyclobutane (**8**) were purchased from Organic Technologies. All other materials 3-chloropropanol (**1**), 4-chlorobutanol (**2**), 5-chloropent-1-yne (**5**), 6-chlorohex-1-yne (**6**), 2.5M n-BuLi in hexane and tetrabutylammonium iodide (TBAI) were purchased from Sigma-Aldrich. All liquid products were subjected to Kugelrohr distillation under reduced pressure using Büchi Glass Oven B-580. Infrared spectra were recorded on a Nicolet 6700 FTIR spectrometer. Nuclear magnetic resonance spectra were recorded on a Brucker Spectrospin DRX 400 MHz Ultrashield™ spectrometer at room temperature using a 5 mm NMR tube. The ^{1}H & ^{13}C spectra were referenced to $CDCl_3$. Samples for elemental analyses were further purified by freeze-thaw distillation. Elemental analyses were carried out on a Perkin Elmer 2400 Series II CHNS/O instrument equipped with an AD6 auto balance.

3-Chloropropyl-4-methylbenzenesulfonate (3): To a cold (~ 0 ºC) chloroform (20 mL) solution of 3-Chloropropanol (**1**, 1.91 g, 20 mmol) is added pyridine (3.17 mL, 39.2 mmol), followed by the addition of p-toluenesulfonyl chloride (5.79 g, 30 mmol) in small portions with constant stirring. The reaction is complete in 2-3 hr as monitored by thin layer chromatography. Ether (60 mL) and water (14 mL) are added. The organic layer is washed successively with 2N HCl, 5% $NaHCO_3$, and water till water layer is neutral (pH=7). The organic layer is dried over anhydrous $MgSO_4$, evaporates and purified by silica gel column using 2% ether/petroleum ether to furnish 4.17 g of **3** in 83% yield.

4-Chlorobutyl-4-methylbenzenesulfonate (4): To a cold chloroform (20 mL) solution (~ 0 ºC) of 4-Chlorobutanol (**2**, 9.33 g, 85.9 mmol) is added pyridine (12.83 mL, 158.6 mmol), followed by the addition of p-toluenesulfonyl chloride (23.42 g, 89.1 mmol) in small portions with constant stirring. After completion of the reaction as monitored by thin layer chromatography, ether (180 mL) and water (60 mL) are added. The organic layer is washed successively with 2N HCl, 5% $NaHCO_3$, and water till water layer is neutral (pH=7). The organic layer is dried over anhydrous $MgSO_4$, evaporates and purified by silica gel column using 2% ether/petroleum ether to furnish 7.43 g of **4** in 85% yield.

1,8-Dichlorooct-4-yne (9): To a cold (-70 ºC) THF (30 mL) solution of 5-chloro-1-pent-yne (**5**, 3.610 g, 35.2 mmol) is added drop-wise n-BuLi (2.5M solution in hexane, 14.0 mL, 35.0 mmol) during a period of 30 minutes. The solution is allowed to warm to room temperature. A solution of 3-Chloropropyl-4-methylbenzenesulfonate (**3**) (8.50 g, 34.2 mmol) in THF (30 mL) followed by tetrabutylammonium iodide (1.26 g, 3.41 mmol) is added to the reaction flask. The reaction mixture is warmed to 70 ºC for 2 hr when the reaction mixture turns thick. The reaction mixture is cooled to 0 ºC, quenched with saturated NH_4Cl and extracted with ether (30 mL x 3). The ether layer is washed sequentially with water till water layer is neutral, brine and dried over anhydrous $MgSO_4$. The liquid obtained after removal of ether, is distilled at 155 ºC /5 mbar to furnish 4.04 g of 1,8-Dichlorooct-4-yne in 66% yield as a liquid.

1,9-Dichloronon-4-yne (10): To a cold (-70 ºC) THF (30 mL) solution of 6-chlorohex-1-yne (**6**, 5.42 g, 46.48 mmol) is added drop-wise n-BuLi (2.5M solution in hexane, 16.9 mL, 42.25 mmol) during a period of 30 minutes. The solution is allowed to warm to room temperature. A solution of 3-Chloropropyl

p-Toluenesulfonate (**3**) (9.66 g, 40.24 mmol) in THF (30 mL) followed by tetrabutylammonium iodide (1.48 g, 4.02 mmol) is added to the reaction flask. The reaction mixture is warmed to 70 ºC for 2 hr when the reaction mixture turns thick. The GC of the reaction mixture showed the absence of the 3-Chloropropyl p-Toluenesulfonate. The reaction mixture is cooled to 0 ºC, quenched with saturated NH_4Cl and extracted with ether (30 mL x 3). The ether layer is washed sequentially with water till water layer is neutral, brine and dried over anhydrous $MgSO_4$. The liquid obtained after removal of ether, is distilled at 85 ºC /40 torr to furnish 4.2 g of 1,9-dichloro-4-nonyne in 56% yield as a liquid.

1,10-Dichlorodec-5-yne (11): To a cold (-70 ºC) THF (60 mL) solution of 6-chlorohex-1-yne (**6**, 6.45 g, 55.32 mmol) is added drop-wise n-BuLi (2.5M solution in hexane, 20.0 mL, 50.00 mmol) during a period of 45 minutes. The solution is allowed to warm to room temperature. A solution of 4-Chlorobutyl p-Toluenesulfonate (**4,** 11.20 g, 45.02 mmol) in THF (60 mL) followed by tetrabutylammonium iodide (2.48 g, 6.70 mmol) is added to the reaction flask. The reaction mixture is warmed to 70 ºC overnight when the reaction mixture turns thick. The GC of the reaction mixture showed the absence of the 4-Chlorobutyl p-Toluenesulfonate. The reaction mixture is cooled to 0 ºC, quenched with saturated NH_4Cl and extracted with ether (50 mL x 3). The ether layer is washed sequentially with water till water layer is neutral, brine and dried over anhydrous $MgSO_4$. The liquid obtained after removal of ether, is distilled at 108 ºC /30 mtorr to furnish 4.5 g of 1,10-dichlorodec-5-yne in 51% yield as a liquid.

(5-Chloropent-1-ynyl)cyclopropane (12): To a cold (-70 ºC) THF (4 mL) solution of ethynylcyclopropane (**7**, 0.556 g, 8.4 mmol) is added drop-wise n-BuLi (2.5M solution in hexane, 2.95 mL, 7.38 mmol) during a period of 30 minutes. The solution is allowed to warm to room temperature. A solution of 3-Chloropropyl p-Toluenesulfonate (**3**) (1.74 g, 7.0 mmol) in THF (6 mL) followed by tetrabutylammonium iodide (0.269 g, 7.38 mmol) is added to the reaction flask. The reaction mixture is warmed to 70 ºC for 2 hr when the reaction mixture turns thick. The reaction mixture is cooled to 0 ºC, quenched with saturated NH_4Cl and extracted with ether (10 mL x 3). The ether layer is washed sequentially with water till water layer is neutral, brine and dried over anhydrous $MgSO_4$. The liquid obtained after removal of ether, is distilled at 100 ºC /50

mbar to furnish 0.80 g of 1-cyclopropyl-5-chloropent-1-yne (**6**) in 80% yield as a liquid.

(6-Chlorohex-1-ynyl)cyclopropane (13): To a cold (-70 ºC) THF (17 mL) solution of ethynylcyclopropane (**7**, 1.47 g, 22.2 mmol) is added drop wise n-BuLi (2.5M solution in hexane, 8.0 mL, 20.0 mmol) during a period of 30 minutes. The solution is allowed to warm to room temperature. A solution of 3-Chlorobutyl p-Toluenesulfonate (**4**) (5.04 g, 19.2 mmol) in THF (6 mL) followed by tetrabutylammonium iodide (0.70 g, 1.90 mmol) is added to the reaction flask. The reaction mixture is warmed to 70 ºC for 2 hr when the reaction mixture turns thick. The reaction mixture is cooled to 0 ºC, quenched with saturated NH_4Cl and extracted with ether (30 mL x 3). The ether layer is washed sequentially with water till water layer is neutral, brine and dried over anhydrous $MgSO_4$. The liquid obtained after removal of ether, is distilled at 132 ºC /50 mbar to furnish 2.19 g of 1-cyclopropyl-5-chlorohex-1-yne (**13**) in 73% yield as a liquid.

(5-Chloropent-1-ynyl)cyclobutane (14): To a cold (-70 ºC) THF (20 mL) solution of ethynylcyclobutane (**8**) (3.00 g, 37.5 mmol) is added drop wise n-BuLi (2.5M solution in hexane, 14.76 mL, 36.9 mmol) during a period of 30 minutes. The solution is allowed to warm to room temperature. A solution of 3-Chloropropyl p-Toluenesulfonate (**3**) (8.72 g, 35.1 mmol) in THF (30 mL) followed by tetrabutylammonium iodide (1.29 g, 36.9 mmol) is added to the reaction flask. The reaction mixture is warmed to 70 ºC for 2 hr when the reaction mixture turns thick. The reaction mixture is cooled to 0 ºC, quenched with saturated NH_4Cl and extracted with ether (10 mL x 3). The ether layer is washed sequentially with water till water layer is neutral, brine and dried over anhydrous $MgSO_4$. The liquid obtained after removal of ether, is distilled at 120 ºC/20 mbar to furnish 3.96 g of **8** in 72% yield as clear liquid.

(6-Chlorohex-1-ynyl)cyclobutane (15): To a cold (-70 ºC) THF (20 mL) solution of ethynylcyclobutane (**8**) (1.90 g, 23.7 mmol) is added drop wise n-BuLi (2.5M solution in hexane, 9.0 mL, 22.5 mmol) during a period of 30 minutes. The solution is allowed to warm to room temperature. A solution of 3-Chlorobutyl p-Toluenesulfonate (**4**) (6.22 g, 23.7 mmol) in THF (30 mL) followed by tetrabutylammonium iodide (0.875 g, 2.37 mmol) is added to the reaction flask. The reaction mixture is warmed to 70 ºC for 2 hr when the reaction mixture turns thick. The reaction mixture is cooled to 0 ºC, quenched

with saturated NH_4Cl and extracted with ether (30 mL x 3). The ether layer is washed sequentially with water till water layer is neutral, brine and dried over anhydrous $MgSO_4$. The liquid obtained after removal of ether, is distilled at 145 ºC/50-20 mbar to furnish 2.95 g of **10** in 73% yield as clear liquid.

1,2-Dicyclopropylethyne (16): *From 1,8-Dichloro-4-Octyne (9):* To a dry THF (60 mL) solution of diisopropylamine (13.90 g, 19.3 mL, 137.4 mmol) is added n-BuLi (2.5 M in hexane, 55.0 mL, 137.5 mmol) at -70 ºC during a period of one hour. The lithium diisopropylamide solution is brought to -10 ºC over a period of time. The LDA solution is transferred via cannula to a jacked dropping funnel at 0 ºC. The LDA solution is added to a dry THF (120 mL) solution of 1,8-dichloro-4-octyne (**9**, 6.00g, 33.5 mmol) at -70 ºC during 45 minutes. The reaction mixture is allowed to warm up to 0 ºC when the GC indicated the completion of the reaction. The reaction mixture is poured on to saturated aqueous NH_4Cl (100 mL) solution. The mixture is extracted with n-pentane (50 mL x 2). The organic layer is washed sequentially with 2% aqueous HCl, aqueous $NaHCO_3$, water till aqueous layer is neutral (pH ≈ 7) and brine solution. The organic layer is dried over anhydrous $MgSO_4$. Removal of solvent furnishes liquid which is subjected to freeze-thaw distillation to furnish 3.27g of 1,2-dicyclopropylacetylene (**13**) in 92 % yield.

From (5-chloropent-1-ynyl)cyclopropane (12): To a dry THF (37 mL) solution of diisopropylamine (6.324 g, mL, 62.5 mmol) is added n-BuLi (2.5 M in hexane, 25.0 mL, 62.5 mmol) at -70 ºC. The lithium diisopropylamide solution is brought to 0 ºC over a period of time. The THF (15 mL) solution of (5-chloropent-1-ynyl)cyclopropane (**12**, 2.85g, 20.0 mmol) is added to LDA solution at -70 ºC during 15 minutes. The reaction mixture is allowed to warm up to -10 ºC during 2 hours. The GC of the reaction mixture indicates the absence of the 1-cyclopropyl-5-chloro-1-pentyne. The reaction mixture is poured on to saturated aqueous NH_4Cl (100 mL) solution. The mixture is extracted with n-pentane (30 mL x 2). The organic layer is washed with water and brine solution sequentially. The organic layer is dried over anhydrous $MgSO_4$. Removal of solvent furnishes liquid which distilled at 80 ºC/50 milibar to furnish 1.80 g of 1,2-dicyclopropylethyne (**11**) in 85 % yield.

(Cyclopropylethynyl)cyclobutane (17) from (5-Chloropent-1-ynyl)cyclobutane (14): To a dry THF (60 mL) solution of diisopropylamine (5.00

g, 49.41 mmol) is added n-BuLi (2.5 M in hexane, 19.8 mL, 49.41 mmol) at -70 ºC during a period of one hour. The lithium diisopropylamide solution is brought to -10 ºC over a period of time. The LDA solution is transferred via cannula to a jacked dropping funnel at 0 ºC. The LDA solution is added to a dry THF (80 mL) solution of (5-chloropent-1-ynyl)cyclobutane (**14**, 2.50g, 15.95 mmol) at -70 ºC during 45 minutes. The reaction mixture is allowed to warm up to 0 ºC and is allowed to stir for 3 hr when the GC indicates absence of **14**. The reaction mixture is poured on to saturated aqueous NH_4Cl (100 mL) solution. The mixture is extracted with n-pentane (50 mL x 2). The organic layer is washed sequentially with water and brine solution. The organic layer is dried over anhydrous $MgSO_4$. Removal of solvent furnishes liquid which is subjected to freeze-thaw distillation to furnish 1.44 g of (cyclopropylethynyl)cyclobutane (**17**) in 75% yield